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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,116	08/30/2000	A. Charles Morgan JR.	180042.418C2	6638

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	18

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/654,116	Morgan et al
Examiner	**Art Unit**
Patricia A. Duffy	1645

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 26, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *19 and 21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *19 and 21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6-26-03 has been entered. It is further noted that the amendment of 5-15-03 has been entered. Claims 19 and 21 are pending and under examination.

Claim Rejections - 35 U.S.C. § 112

2. Claims 19 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a growth blocking agent that binds a vitamin B12 binding site on transcobalamin II (TcII), the agent being capable of competitively antagonizing or modulating said binding site to inhibit the cellular uptake of vitamin B12 wherein the agent is a monoclonal antibody. The specification fails to teach what residues on TcII are

responsible for vitamin B12 binding and does not set forth the regions on the TcII polypeptide that are binding sites for vitamin B12. Moreover, the prior art at the time of invention does not set forth the regions on the TcII polypeptide that are binding sites for vitamin B12. Therefore, one skilled in the art would not know what immunogen to use to make antibodies directed to such. Further, one skilled in the art would be unable to predict what potential binding sites would be appropriate to target for the identification of antagonists or modulators. The specification fails to teach even a single monoclonal antibody molecule that could be modified to bind and antagonize. Without out guidance as to the structure of such molecules that are directed to the vitamin B12 binding site on TcII, one of skill in the art would have to screen for potential candidates. However, the specification fails to teach what the binding site of vitamin B12 on TcII encompasses and as such one would have to resort to screening using apo-TcII. However, it has been well established in the art that screening of agents that bind to receptors, or in this case agents that bind to binding proteins, do not have the ability to determine agonists versus antagonist function, and the art establishes difficulty of excluding "non-specific" inhibition of receptor binding (page 102, first full paragraph, Burch, R.M.., Journal of Receptor Research, 11(1-4):101-113, 1991). The state of the art does not allow for accurate design of molecules based solely on function and an undisclosed binding site (vitamin B12 binding site on TcII). Rudinger et al "Peptide Hormones" ed by Parsons et al, University Park Press June

1976, pages 1-7, especially page 6, teaches that "the significance of particular amino acids and sequences for different aspects of biological activity can not be predicted a priori but must be determined from case to case by painstaking experimental study.". Kuntz et al (Science 257:1078-1082, 1992) discloses that with current technology scientists can not yet design drugs from "first principles" (e.g. page 1078, left column). Though Kuntz et al disclose a particular computational cycle used to combine structural information regarding complemenatrity between designer drug and target, the method (a) uses X-ray crystallographic or computer generated structural data not set forth in this specification and are known in the art to involve non-routine experimentation and/or results of such are not predictive of *in vivo* activities, (b) of the 100,000 molecules modeled, only 2-20% of 10-50 compounds might show the predicted biological properties, and (c) the method is characterized by Knutz et al as "problematic" in optimizing leads (e.g. doe to difficulties in obtaining proper ligand conformation and discriminating among several proposed interaction modes of similar energy (see e.g. 1059-1061 "Structure-based design"). Further, the same authors question whether the technique will work for compounds other than peptides and oligonucleotides (e.g. page 1061, left column "...it is possible to adapt...) and the algorithm is designed for enzyme inhibitors, in contrast to the instant invention. The assays disclosed in the specification do not provide for all the functional information recited in the claims (directed to the vitamin B12 binding site on TcII, growth blocking, antagonizing or

modulating the binding site). The courts have held that "... whenever there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of the invention in order to constitute adequate enablement." *Genetech Inc. v. Novo Nordisk A/S* 42USPQ2d 1001.

In the absence of further guidance from Applicants relating to the above noted deficiencies, it would require undue experimentation to make and use the claimed monoclonal antibody growth blocking agent.

3. Claims 19 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require a growth blocking agent that is binds to a vitamin B12 binding site on TcII. Neither the claims nor the specification teaches the metes and bounds of the vitamin B12 binding site on TcII, as such the metes and bounds of agents that bind to this site as claimed can not be readily ascertained.

The meaning of "antagonizing or modulating said binding site is unclear because in the art the terms "antagonize or modulate" refer to functions, not sequences or sites. An

effector function may be antagonized or binding of a natural ligand may be antagonized by addition of an antagonists, however, the binding site itself is not antagonized. Additionally, the specification nor the claims defines the term "modulating" as it relates to binding the vitamin B12 binding site on TcII.

4. Claims 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Quadros et al (Blood et al, 10(Suppl 1) p 125A, December 1-5, 1995.

Quadros et al teach monoclonal antibodies that block vitamin B12 binding to apo TcII and decrease the uptake of vitamin B12 (see entire abstract). Quadros et al teaches that these monoclonal antibodies bind "at or near" the vitamin B12 binding site on apo TcII.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

5. Any art cited herein has been previously provided to Applicants in the prosecution history of this application.

Status of Claims

6. No claims are allowed.

7. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Thursday and Saturday from 10:30 AM to 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
September 10, 2003

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600